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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,789	07/26/2001	Lieping Chen	07039-219001	6835

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/915,789	Applicant(s) CHEN, LIEPING	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)[·] Responsive to communication(s) filed on *27 November 2002 and 13 January 2003* .

2a)[ ] This action is **FINAL**. 2b)[×] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *4-6,10-31 and 34-52* is/are withdrawn from consideration.

5)[ ] Claim(s) _____ is/are allowed.

6)[·] Claim(s) *1-3,7-9,32 and 33* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[·] The specification is objected to by the Examiner.

10)[·] The drawing(s) filed on *13 January 2003* is/are: a)[×] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[×] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [·] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [·] Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) [ ] Interview Summary (PTO-413) Paper No(s). _____ .
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: .

DETAILED ACTION

1. Claims 1-52 are pending.

2. Applicant's election without traverse of Group I in Paper No. 12 is acknowledged.

Claims 4-6, 10-31 and 34-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3, 7-9 and 32-33 *are under consideration in the instant application.*

Drawings

3. The formal drawings submitted 1/13/03 have been approved by the Draftsman.

Priority

4. Provisional application 60/220,991 appears to provide adequate written support for the instant claims.

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

In addition, Applicant should avoid the use of novel in the title, as patents are presumed to be novel and unobvious.

6. Applicant should avoid the use of novel in the abstract, as patents are presumed to be novel and unobvious.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. The disclosure is objected to because it contain an embedded hyperlink *at least* on page 14 at line 14. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Applicant is requested to review the application for additional embedded hyperlinks and/or other forms of browser-executable code and delete them. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. See MPEP § 608.01 and 608.01(p).

9. For examination purposes, it is noted that "has" and "having" are considered "open", i.e., "comprising" language.

Claim Rejections - 35 USC § 112 second paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) In claim 1, the phrase "encodes a polypeptide with an amino acid sequence *with* SEQ ID NO:5" fails to set forth the metes and bounds of the claimed subject matter because it is unclear as to the relationship of SEQ ID NO:5 to the encoded polypeptide. Applicant is requested to clarify this relationship. The following claim language is suggested as one possible means of setting forth the metes and bounds of the claimed subject matter: -- encodes a polypeptide with the amino acid sequence set forth in SEQ ID NO:5 -- .

Similarly, in claim 2 the phrase "encodes a polypeptide comprising an amino acid sequence *with* SEQ ID NO:5" fails to clearly set forth the metes and bounds of the claimed subject matter. It is suggested that Applicant amend the phrase to recite -- encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:5 --.

B) Claim 1 is indefinite in the recitation of "stringent conditions" as it is unclear to what conditions the claims are drawn. Stringency of hybridization condition can be considered either "low", "moderate", or "high"; encompass both salt concentrations and temperature of hybridization; and determine the degree of complementarity needed for one nucleic acid molecule to hybridize to another. Absent a clear definition as to these parameters, the claims are indefinite as it cannot be determined what type of hybridization conditions are encompassed by the instant claims, in turn prohibiting a determination of the degree of complementarity possessed by the nucleic acid sequence which hybridizes to the complement of SEQ ID NO:5.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid that:

encodes SEQ ID NO:5,

encodes a protein with the ability to costimulate a T cell and hybridizes under defined high stringency conditions to the full length complement of the nucleic acid of SEQ ID NO:6,

as well as for vectors and host cells comprising these nucleic acid sequence, and methods of producing a polypeptide encoded by these nucleic acid sequence, and

fragments of SEQ ID NO:6 that do not comprise/"have" undefined flanking sequences:

does not reasonably provide enablement for a nucleic acid that:

hybridizes under "stringent" conditions,

"fragments" of SEQ ID NO:6 that comprises undefined flanking sequence, or

nucleic acids that "hybridize to a fragment" of SEQ ID NO:5.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The instant claims encompass in their breadth *any* nucleic acid that shares some minimal degree of structural relatedness to the nucleic acid of SEQ ID NO:6 by virtue of being encoded by a nucleic acid which "hybridizes under stringent conditions" to the complement of a sequence that encodes SEQ ID NO:5, or that is a fragmentary sequence of any of these "related" polypeptides; so long as the related nucleic acid encode a polypeptide or fragment thereof possesses the ability to co-stimulate a T cell. Thus the breadth of the instant claims is extensive, encompassing numerous structural and functional variants of the nucleic acid of SEQ ID NO:6 and nucleic acids encoding SEQ ID NO:5.

Applicant has disclosed a nucleic acid sequence (SEQ ID NO:6) encoding a B7-H4 polypeptide (SEQ ID NO:5) which has the ability to costimulate T cells (e.g., pages 33-34 of the specification).

However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the numerous variants and fragments of SEQ ID NO:6 encompassed by the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for costimulation of T cells.

Further, the fact that two nucleic acid sequences will hybridize under some undefined "stringent conditions" does not in and of itself require that polypeptides encoded by the two sequences/sequence complements share any functional activity. It was well know in the art at the time the invention was made that hybridization could occur between *f*ragments of two sequences, and so does not require that the full length of a referenced SEQ ID NO: be shared. Thus a great deal of sequence variability with respect to the full-length nucleic acid is possible, leading to extensive variation in the encoded polypeptide. Finally, hybridization under conditions other than high stringency would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that polypeptides encoded by the hybridizing sequences/sequence complements would share any function.

Thus hybridization language in the absence of limitations regarding both the hybridization conditions and the sequence length over which the hybridization takes place does not allow the skilled artisan to make and use polypeptides encoded by hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation. Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the skilled artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

The requirement for high stringency hybridization conditions and hybridization over the full length is further emphasized in the instant example since, as summarized in Figures 2 and 3 of Coyle et al. (Nature Immunol. 2:203-209 2001) the B7-like family members have distinct expression patterns and distinct functions, *even though they share some degree of similar overall structure*. The skilled artisan was well aware that even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 (B7-1) and CD86 (B7-2 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides differing even in only conservative substitutions.

In addition, the instant claims encompass fragments of the aforementioned nucleic acids due to the absence of a requirement that hybridization be over the full length; and in view of the use of "a" and "an", indefinite articles which when used in contexts such as "an amino acid sequence of ..." indicates that subsequences of polypeptides encoded by the referenced SEQ ID NO: are also encompassed by the claim language. Although Applicant has provided a working example of a fragment comprising the extracellular domain which can enhance T cell proliferation (e.g., pages 33-34), the skilled artisan would not be able to reasonably predict without undue experimentation which other fragments of SEQ ID NO:5 would share this activity and thus would not be able to predict which fragments of encoding nucleic acids including SEQ ID NO:6 would encode for this activity. In addition, it would be even more unpredictable as to which fragments of the "variants" of SEQ ID NO:6 encompassed by the hybridization and substitution language would encode polypeptides that costimulate T cells.

Thus although the level of skill in the art is high, without detailed direction as to which sequences and sequence lengths are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of sequences encompassed by the instant claims would encode the disclosed function of the polypeptide of SEQ ID NO:5. Without sufficient guidance, the changes which can be made in these nucleic acids and still encode polypeptides that have the ability to co-stimulate a T cell are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

14. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following written description rejection is set forth herein.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant has disclosed a single nucleic acid sequence (SEQ ID NO:6) encoding a B7-H4 polypeptide (SEQ ID NO:5) which has the ability to costimulate T cells (e.g., Examples 5 and 6 on pages 33-34 of the specification).

The instant claims are drawn to an extensive genus of nucleic acids encompassing any nucleic acid that encodes a polypeptide or fragment thereof which share some minimal degree of structural relatedness to the polypeptide of SEQ ID NO:5, or fragment thereof, by virtue of being encoded by a nucleic acid which "hybridizes under stringent conditions".

The claims only require that these nucleic acid sequences have the ability to co-stimulate T cells. This functional limitation does not further describe the large genus of nucleic acids encompassed by the broad structural limitations of the claims to the extent that a single species, SEQ ID NO:6, could be considered "representative" of the genus. It is noted that other polypeptides have the ability to costimulate T cells, yet share only minimal sequence identity with the instantly encoded polypeptide of SEQ ID NO:5. Thus the recitation of the functional limitation that a nucleic acid of the invention encodes a polypeptide that costimulates T cells still encompasses a large number of sequences that have not been described in the specification. Claims 2 and 3 are included in the instant rejection because the instant claim language reads on fragmentary sequences (encodes..."*an* amino acid sequence with SEQ ID NO:5", "*a* sequence of SEQ ID NO:6") and the DNA of claim 1 comprises these sequences.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicant is also directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections – 35 U.S.C. § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 102(a) as being anticipated by Baker et al. (WO99/63088, IDS #AL).

Baker et al. teach the DNA encoding the membrane-bound protein PRO1219. The DNA encoding PRO1291 is 100% identical to the full length sequence of instant SEQ ID NO:6 (compare SEQ ID NO:6 to the sequence shown in Figure 207) .

Baker et al. also teach vectors comprising the DNA, host cells comprising said vectors and method for expressing the protein encoded by the DNA (e.g., page 280). The vectors taught must include those in which the nucleic acid is operably linked to a regulatory element to permit expression of the sequence because expression of the polypeptide is explicitly taught. Given that the PRO1219 protein is the same protein encoded by instant SEQ ID NO:6, the co-stimulation of T cell proliferation would be an inherent functional property of the encoded PRO1291 polypeptide.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the DNA encoding the PRO1291 polypeptide.

The reference teachings thus anticipate the instant claimed invention.

17. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Mitcham et al. (US Pat. No. 6,468,546, see columns 1-34 and 305-312).

Mitcham et al. teach the DNA of SEQ ID NO:391, encoding ovarian carcinoma protein of SEQ ID NO:393. The DNA encoding SEQ ID NO:393 is 100% identical to the full length sequence of instant SEQ ID NO:6 (compare SEQ ID NO:6 to the sequence shown in SEQ ID NO:391) .

Mitcham et al. also teach vectors comprising the DNA, host cells comprising said vectors and method for expressing the protein encoded by the DNA (e.g., columns 9 and 12). The vectors taught must include those in which the nucleic acid is operably linked to a regulatory element to permit expression of the sequence because expression vectors and expression of the polypeptide are explicitly taught at column 12, especially lines 3-21. Given that instant SEQ ID NO:6 and SEQ ID NO:391 of Mitcham et al. encode identical proteins, co-stimulation of T cell proliferation would be an inherent functional property of the polypeptide of SEQ ID NO:393 encoded by SEQ ID NO:391 of Mitcham et al.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the DNA encoding the polypeptide of SEQ ID NO:393 of Mitcham et al.

The reference teachings thus anticipate the instant claimed invention.

18. Claims 1-3, 7-9 and 32-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Fox et al. (US 2002/0165347, see entire document).

Fox et al. teach the DNA of SEQ ID NO:1, encoding the B7-L protein of SEQ ID NO:2. The DNA of SEQ ID NO:1 encoding SEQ ID NO:2 is 100% identical over the full length coding region of instant SEQ ID NO:6 (compare SEQ ID NO:6 to the sequence shown in SEQ ID NO:1 as encoding SEQ ID NO:2) .

Fox et al. also teach vectors comprising the DNA, host cells comprising said vectors and method for expressing the protein encoded by the DNA (e.g., paragraphs 146-206 and claims). The vectors taught include those in which the nucleic acid is operably linked to a regulatory element to permit expression of the sequence (e.g., paragraphs 157-180). Given that instant SEQ ID NO:6 and SEQ ID NO:1 of Fox et al. encode identical proteins, co-stimulation of T cell proliferation would be an inherent functional property of the polypeptide of SEQ ID NO:2 encoded by SEQ ID NO: 1 of Fox et al.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the DNA of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:2 of Fox et al.

The reference teachings thus anticipate the instant claimed invention.

Conclusion

19. No claim is allowed.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
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January 31, 2003

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